Remarks

Reconsideration of this Application is respectfully requested.

Upon entry of the foregoing amendment, claims 215-219, 221-235, 237-249, 251-265, 267-279 and 281-292 are pending in the application, with 215, 231, 245, 261 and 275 being the independent claims. Claims 220, 236, 250, 266 and 280 are sought to be canceled without prejudice to or disclaimer of the subject matter therein.

These changes are believed to introduce no new matter, and their entry is respectfully requested. Support for the amendment to claims 215, 231, 245, 261 and 275 adding the limitation "wherein the amino acids of said polypeptide corresponding to amino acids 192 to 197 of SEQ ID NO:4 have been deleted," can be found in previous claims 220, 236, 250, 266, 280 and the specification at paragraph [0169]. Accordingly, no new matter has been added by these amendments.

Based on the above amendment and the following remarks, Applicant respectfully requests that the Examiner reconsider all outstanding objections and rejections and that they be withdrawn.

Claim Objection.

The Examiner objects to claims 231 and 261 under 37 CFR 1.75 as being substantial duplicates of claims 215 and 245. (Office Action, hereinafter "OA," at page 8.) Specifically, claims 231 and 261 are directed to "reduce the severity of anthrax" while claims 215 and 245 are directed at "prevention." Applicants respectfully traverse this objection.

The finding that claims 231 and 261 are substantially duplicates of claims 215 and 245 appears to be inconsistent with the Examiners assertion that claims 231 and 261

encompass an enabling disclosure while maintaining that claims 215 and 245 are allegedly not enabled. While not agreeing with the Examiner's enablement rejection the interpretations of the claims by the Examiner is evidence that the subject matter of the claims differ. "Court decisions have confirmed applicant's right to restate (*i.e.*, by plural claiming) the invention in a reasonable number of ways. Indeed, a mere difference in scope between claims has been held to be enough." (*See* MPEP 706.03(k).) Thus, the assertion by the Examiner that one set of claims is enabled while the other set of claims is allegedly not enabled is evidence that the claims have a different scope. As such, it is respectfully requested that the Examiner withdraw the objection.

Rejections under 35 U.S.C. § 112

35 U.S.C. § 112, first paragraph (scope of enablement)

The Examiner has rejected claims 215-292 under 35 U.S.C. § 112, first paragraph. (OA at pages 2.) The Examiner asserts that the specification while "being enabling to reduce the severity of anthrax infection" in a mammal, does not reasonably provide enablement for a method of "preventing anthrax infection." (OA at pages 3, line 5.) Specifically, the Examiner asserts that the term "not only embrace a range of outcomes from lessening the severity of disease but also encompasses complete cure from the infection." (OA at page 4) (internal citation omitted). Applicant respectfully traverses this rejection.

The test of enablement is whether one reasonably skilled in the art could make or use the invention from the disclosure in the specification coupled with information known in the art without undue experimentation. *In re Wands*, 858 F.2d 731, 737 (Fed. Cir. 1988). The captioned application has provided working examples in which three

species of animals have been immunized with the claimed DNA based vaccine and all three species have mounted an immune response to protective antigen (hereinafter "PA"), using the PA encoding DNA that is human codon optimized. In challenge experiments all animals that were given the DNA based vaccine survived while all control animals died. (*See* Examples 12, 13 and 16.) Because the animals survived the challenge experiments, Applicant asserts that the captioned application is enabled for methods of preventing anthrax infection.

i. prevention / cure

The Examiner asserts there is enablement in the specification for the limitation "to reduce the severity of anthrax" (OA at page 2) but not sufficient enablement for a method of "preventing anthrax infection." (OA at page 3, line 5.) Further, the Examiner asserts that the definition provided in the specification included prevention, cure, retard or reduce the severity of anthrax. "Therefore, contrary to applicants assertion that the term not only embrace a range of outcome from lessening the severity of the disease to the prevention of infection but also encompasses complete cure from infection." (OA at page 4.) Applicant respectfully traverses this rejection.

Ordinarily the wording of a claim is given the "plain and ordinary meaning," unless the specification defines the words differently. (*See* MPEP § 2111.01.) It is Applicant's position that the terms "treatment or prevention" in the captioned application are consistent with the art recognized use of these terms. "[T]he ordinary and customary meaning of a claim term is the meaning that the term would have to a person of ordinary skill in the art in question at the time of the invention, *i.e.*, as of the effective filing date of the patent application." *Phillips v. AWH Corp.*, 415 F.3d 1303, 1313 (Fed. Cir. 2005)

(en banc). (*See* MPEP § 2111.01.) Additionally, the Examiner is reminded that breadth of a claim does not make a claim not enabled or indefinite as long as the scope of the subject matter that is embraced is clear. *In re Miller*, 441 F.2d 689 (CCPA 1971). (*See* MPEP 2173.04.)

The Examiner takes the position that the term preventing anthrax infection "not only embrace a range of outcomes from lessening the severity of disease but also encompasses complete cure from the infection." (OA at page 4) (emphasis added). The word of a claim must be given their "plain meaning" unless such a meaning is inconsistent with the specification. (*See* MPEP §2111.01) The Examiner has taken the position that "claims directed to prevention are given the full breadth as per the specific definition set forth in the specification ranging from cure to reducing severity of disease." (OA at page 5.) The Examiner asserts that the claims are not enabled for "complete cure from infection." (OA at page 4.) The Examiner asserts that case law requires that any special meaning must be sufficiently clear in the specification, citing *Toro Co. v. White Consolidated Industries Inc.*, 199 F.3d 1295, 1301 (Fed. Cir. 1999) and *Multiform Desiccants Inc. v. Medzam Ltd.*, 133 F.3d 1473, 1477 (Fed. Cir. 1998). Here the specification specifically recites that "[i]t is not required that any composition of the present invention provide total immunity to *B. anthracis* or **totally cure** or eliminate all anthrax disease symptoms." (*See* paragraph [0116]) (emphasis added). The wording of a claim is either given the "plain and ordinary meaning" or the "special meaning" as defined the specification. Here the Examiner is not using the complete definition of what is encompassed by the term "cure" as provided in the specification. The specification is clear that the composition, and methods of using the composition,

does not have to totally cure or eliminate anthrax disease. Thus, an interpretation that "cure" means "complete cure from infection" is contrary to the definition provided in the specification that says it is not required that the composition provide total immunity, totally cure or eliminate all anthrax disease symptoms. Here the Examiner looks to the specification to interpret that the term "prevent" encompasses "cure," and then asserts that the specification is not enabled for "complete cure of infection" as interpreted under the plain and ordinary meaning. This interpretation is contrary to the definition found in the specification.

It remains Applicant's position that the terms "prevent" in the captioned application is consistent with the art recognized use of this term. However, if the Examiner wishes to apply the definition of the meaning as provided in the specification, then the Examiner needs to use the complete definition as set out in the specification and randomly not pick and choose between the plain and ordinary meaning and the meaning as used in the specification. Where an explicit definition is provided in the specification, as it is here, that definition controls. *See Toro Co. v. White Consolidated Industries Inc.*, 199 F.3d 1295, 1301 (Fed. Cir. 1999) The specification defines the term to prevent or treat, *i.e.* cure, ameliorate, lessen the severity of, or prevent or reduce contagion of infectious disease caused by *B. anthracis.* (*See* specification, paragraph [0057].) More importantly, the specification is clear that "**it is not required that any composition of the present invention provide total immunity to *B. anthracis* or totally cure or eliminate all anthrax disease symptoms.**" (*See* specification, paragraph [0116]) (emphasis added). Even so, the Examiner continues to interpret the term "cure" to be "complete cure from the infection," this interpretation is clearly contrary to the definition

provided in the specification. Here the Examiner is looking to the specification to define the term "prevent," yet the Examiner fails to look to the specification to determine what is encompassed by the term "cure." This is contrary to case law which provides that either the plain and ordinary meaning is applied to the wording of a claim or the definition provided specification is used. Here, the specification is clear that the composition does not have to provide total immunity, totally cure or eliminate all anthrax disease symptoms. Applicant respectfully requests reconsideration and withdrawal of this rejection.

ii. administration via any route

The Examiner alleges that it would require extensive experimentation to carry out the claimed method. (OA at pages 7.) Specifically, the Examiner asserts the specification or cited art "does not provide any evidence that compositions comprising (GAP-DMORIE) and any co-lipid administered via any route would elicit immune response to a level sufficient to reduce severity of anthrax infection as exemplified in the instant application." (OA at page 6) (emphasis added) The Examiner appears to doubt whether the ordinary artisan would be able to treat or prevent anthrax by administering the vaccine using a route of administration not exemplified in the specification. Applicants respectfully traverse this rejection.

The Examiner takes the position that every conceivable route of administration must be proven effective for the specification to be enabled. Claims can encompass inoperative embodiments. (*See* MPEP 2164.08(b).) Here, the specification has exemplified one route of administration, intramuscular injection, in three different animals (mouse, rabbit, monkey). Additionally, the specification discloses an example

of intramuscular injection followed by electroporation to facilitate DNA uptake by cells. The presence of inoperative embodiments within the scope of a claim does not necessarily render a claim nonenabled. *Atlas Powder Co. v. E.I. du Pont de Nemours & Co.*, 750 F.2d 1569, 1577, (Fed. Cir. 1984) (prophetic examples do not make the disclosure nonenabling). A disclosure of a large number of operable embodiments and the identification of a single inoperative embodiment did not render a claim broader than the enabled scope because undue experimentation was not involved in determining those embodiments that were operable. *In re Angstadt,* 537 F.2d 498, 502-503, 190 USPQ 214, 218 (CCPA 1976) The specification has exemplified the prevention of anthrax infection in three animals, mouse, rabbit and monkey. Here, Applicant has shown in three animal models that the instantly claimed vaccine formulation induced an immune response in each animal. Applicant has shown that that the vaccine provides complete protection in the animals when challenged with a lethal dose of anthrax. (*See* specification paragraphs [0239-0248].)

Examples 12, 13 and 16 of the captioned application describe immunization and challenge experiments in rabbits. Indeed, all animals that were immunized with SEQ ID NO:7, a human codon optimized nucleic acid sequence encoding amino acids 199-764 of SEQ ID NO:4 with a deleted furin cleavage site, and Vaxfectin or DMRIE/DOPE survived anthrax spore challenge as described in Table 17. Applicant has shown that immunization with an anthrax DNA vaccine can provide protective immunity in at least 40 animals. (*See* specification Table 17.) Additionally, the animals tested were subjected to aerosolized anthrax spore challenge which is "the gold standard for anthrax vaccine efficiency because it exposes the animal to the agent and expected mode of

delivery anticipated in the event of a bioterrorist attack." (Hermanson, *et al. Proc. Natl. Acad. Sci.* 101:13601-13606 (2004), at page 13605, document previously listed as NPL4 on IDS submitted August 26, 2006.) "A cationic lipid-formulated plasmid DNA vaccine confers sustained antibody-mediated protection against aerosolized anthrax spores." (*Id.* at page 13604-13605.)

The Examiner cites McCulskie *et al.* "not to show the feasibility of administration of anthrax vaccine rather it is cited to provide general evidence that administration of plasmid DNA by different route resulted in varying immune response." (OA at page 7.) A varying immune response is still within the scope of the claims. The specification is clear that "it is not required that any composition of the present invention provide total immunity to *B. anthracis* or totally cure or eliminate all anthrax disease symptoms." (*See* specification, paragraph [0116].) McCulskie *et al.* shows that the most common routes of vaccine administration intramuscular, intervenous, sublingual and intradermal all produce good antibody titer and good CTL response to a DNA vaccine. Even if the immune response via other routes is not predicable, the testing of an immune response to a particular route of administration falls with the skill of the ordinary artisan. Thus, the experimentation that may be required is not undue.

The quantity of experimentation that may be required is not the bench mark for determining whether the experimentation is "undue." (*See* MPEP 2164.06.) "[A]n extended period of experimentation may not be undue if the skilled artisan is given sufficient direction or guidance." *In re Colianni,* 561 F.2d 220, 224, (CCPA 1977). 'The test is not merely quantitative, since a considerable amount of experimentation is permissible" *In re Wands*, 858 F.2d 731, 737, (Fed. Cir. 1988) Here the specification has

provided guidance as to how to make the composition "comprising a nucleic acid fragment which encodes a polypeptide at least 97% identical to amino acids 199 to 764 of SEQ ID NO:4, wherein the amino acids of said polypeptide corresponding to amino acids 192 to 197 of SEQ ID NO:4 have been deleted" and has provided guidance as to how a person of ordinary skill in the art would go about testing the composition.

Applicant reiterates that the claimed methods do not require any specific level of immune response other than to reduce the severity or prevent anthrax infection as defined in the specification, *e.g.* at paragraphs [0057] and [0116]. Certainly, the claimed methods do not require an "optimal immune" response as the examiner is requiring. (OA at page 6.) The data in the Nagata *et al.* reference showed some level of immune response in all DNA plasmids tested, including the plasmid which had the native codon usage. (Nagata *et al.*, *Biochem. Biophys. Res. Comm.* 261:445-451 (1999), see Fig. 3.) Moreover, Applicant asserts that based on the teaching in the specification, it would have been routine experimentation for one of skill in the art to test various codon optimized polynucleotides in the mouse, rabbit and primate animal models described in Examples 10-13 and 15 or in the assays described in Example 9 of the present application to determine which variants could treat or prevent anthrax infection. Applicant respectfully requests reconsideration and withdrawal of this rejection.

iii. effective immune response with 97% identity to SEQ ID NO:4

Applicant thanks the Examiner for withdrawing this part of the rejection. (OA at page 5.)

iv. DNA delivery

The Examiner asserts that the specification does not provide "any evidence that a composition comprising (GAP-DMORIE) and any co-lipid administered via any route would elicit immune response to a level sufficient to reduce severity of anthrax infection as exemplified in the instant application." (OA at page 6.) The Examiner asserts that there is a need for an "optimal immune response" for the prevention or reduction of severity of anthrax infection." (OA at page 6.) Applicant respectfully traverses this rejection.

The Examiner cites Dass *et al.* for the proposition that lipoplex-mediated gene delivery can be toxic. Cationic lipid-DNA complexes "has shown varying degree of success, primarily due to toxicity associated with these formulations." (OA at page 7.)

The Examiner asserts that the reference of Ferrari *et al.* "does not provide any evidence that composition comprising (GAP-DMORIE) and any co-lipid administered via any route would elicit immune response to a level sufficient to reduce severity of anthrax infection as exemplified in the instant application." (OA at page 6.)

The Examiner cites McCulskie *et al.* "not to show the feasibility of administration of anthrax vaccine rather it is cited to provide general evidence that administration of plasmid DNA by different route resulted in varying immune response." (OA at page 7.) A varying immune response is still within the scope of the claims. The specification is clear that "it is not required that any composition of the present invention provide total immunity to *B. anthracis* or totally cure or eliminate all anthrax disease symptoms." (*See* specification, paragraph [0116].) McCulskie *et al.* shows that the most common routes of vaccine administration intramuscular, intervenous, sublingual and intradermal

all produce good antibody titer and good CTL response to a DNA vaccine. Even if the immune response via other routes not predicable, the testing of an immune response to a particular route of administration falls with the skill of the ordinary artisan and is easily testable. Thus, the experimentation that may be required is not undue.

Applicant respectfully asserts that the Examiner is requiring an unreasonable scope of enablement standard. The Federal Circuit has stated that the PTO has the burden of initially showing that Applicant's disclosure suggests "an inherently unbelievable undertaking or involve[s] implausible scientific principles." *In re Brana*, 34 USPQ 2d 1436, 1441 (Fed. Cir. 1995). The documents cited by the Examiner do not meet this burden.

Applicant respectfully reminds the Examiner that the proper standard for compliance with enablement, scope of enablement, is not *absolute predictability* but *objective enablement*; evidence need not be *conclusive* but merely *convincing*. Accordingly, Applicant submits that the compelling animal data presented in the specification is sufficiently convincing that one of ordinary skill in the art would not doubt the feasibility of the claimed invention. Moreover, the *in vivo* successes documented in the Examples of the instant specification, *e.g.* Examples 10-13, clearly outweigh any speculative allegations of unpredictability asserted by the Examiner.

According to the Examiner's apparent view of the scope of enablement requirement, an applicant would have to submit conclusive data from human clinical trials in order to adequately enable a method of treatment applicable to humans. Clearly exposing humans to anthrax in human clinical trials is highly unethical and is not required by the FDA for approval of an anthrax vaccine. (*See* 67 Fed. Reg. 37989, May

31, 2002, previously provided in the response of September 11, 2006.) In addition, this is clearly in conflict with the statute, the rules and the guidelines of the M.P.E.P. Specifically, under the current case law, clinical efficacy is not required to show that a therapeutic process is operable. As stated in M.P.E.P. § 2107.01, the "courts have found utility for therapeutic inventions, despite the fact that an applicant is at a very early stage in the development of a therapeutic regimen" or that a therapeutic treatment regimen is not at a stage where it is ready to be practiced on humans. *Cross v. Iizuka*, 753 F.2d 1040, 224 U.S.P.Q. 739 (Fed. Cir. 1985); *In re Brana*, 51 F.3d 1560, 34 U.S.P.Q.2d 1436 (Fed. Cir. 1995).

It is not within the province of the USPTO to require proof of efficacy in animals, let alone humans, to grant a patent including claims to therapeutic methods. The FDA will accept evidence from animals studies to provide substantial evidence of the effectiveness of products, when human efficacy studies are not feasible. For the FDA approval purposes it is sufficient to establish the effect in either more than one animal, or in a single well-characterized animal model that has been shown to predict the human response. (*See* 67 Fed. Reg. 37989, May 31, 2002, previously provided in the response of September 11, 2006.) The PTO guidelines do not require proof of efficacy, in fact are explicit on this point: "Office personnel should not impose on applicants the unnecessary burden of providing evidence from human clinical trials. There is no decisional law that requires an applicant to provide data from human clinical trials to establish utility for an invention related to treatment of human disorders." (M.P.E.P. § 2107.03). The guidelines further state that "[t]he Office must confine its review of patent applications to the statutory requirements of the patent law, and in quoting *In re Brana*, *supra*, that

"FDA approval, however, is not a prerequisite for finding a compound useful within the meaning of the patent laws". *Id.* In fact, all that is required by the patent laws is that a "*reasonable correlation*" exist between the scope of the claims and the scope of enablement. Citing to M.P.E.P. § 2164.02, "'correlation' as used herein refers to the relationship between *in vitro* or *in vivo* animal model assays and a disclosed or a claimed method of use." If a particular model is recognized as correlating to a specific condition, then it should be accepted as such unless the Examiner has evidence that the model does not correlate. *In re Brana, supra* at 1566. Since the initial burden is on the Examiner to give reasons for lack of enablement, the Examiner must also give reasons for a conclusion of lack of correlation for an *in vitro* or *in vivo* animal model example. As stated in *Cross v. Iizuka*, *supra*, at 1050, a rigorous or an invariable exact correlation is not required.

The references cited by the Examiner and arguments set forth do not cast doubt on the feasibility of the claimed invention in light of the data presented in the specification. Indeed, the captioned application describes various *in vitro* assays known in the art which sufficiently correlate to *in vivo* anthrax challenge experiments, *e.g.* at paragraph [0155] of the specification. The specification also describes data for various vaccine compositions in three different animal models. (*See* Examples 10-13 and 15.) Furthermore, the captioned application contains data showing that DNA vaccines containing codon optimized polynucleotides encoding anthrax antigens can provide protective immunity in rabbits. (*See* Example 13.) Finally, post-filing art, co-authored by the inventor of the captioned application, reports that the rabbit studies described herein resulted in product selection, pre-clinical safety studies, and a U.S. FDA

Investigational New Drug allowance. "A cationic lipid-formulated plasmid DNA vaccine confers sustained antibody-mediated protection against aerosolized anthrax spores." (*See* Hermanson, *et al. Proc. Natl. Acad. Sci.* 101:13601-13606, 1306 (2004).) Applicant asserts that a reasonable correlation thus exists between the data provided in the captioned application and the claimed methods.

Thus, given the explicit disclosure of specific *in vivo* working examples, using models that reasonably correlate to mammals, as noted in paragraph [0155] of the specification, Applicants respectfully submit that one skilled in the art would be able to make and use the claimed invention without undue experimentation. Applicant respectfully asserts that this rejection be withdrawn.

For the reasons given above, Applicant submits that the scope of the present claims is commensurate in scope with the enablement provided in the present specification. The considerations listed by the Examiner are either resolved by the teachings in the specification or would have required only routine experimentation by one of skill in the art to practice the claimed invention. Accordingly, Applicant requests reconsideration and withdrawal of the scope of enablement rejection in view of the amendments to the claims and the remarks herein.

Rejections under 35 U.S.C. § 103

The Examiner has rejected claims 215-292 under 35 U.S.C. § 103(a) as being unpatentable over Lee *et al.* (U.S. Pat. App. No. 2004/0009945, publication date January 15, 2004, effective filing date July 10, 1998); Nagata *et al.* (Biochemical Biophysical Research Comm. 1999, Vol. 261, No. 2, pages 445-451; hereinafter "Nagata") and Hartikka *et al.* (Vaccine 2001, Vol. 19, pages 1911-1923; hereinafter "Hartikka"). (OA

at pages 9.) More specifically, the Examiner stated that Lee *et al.* emphasize that it would be routine "to optimize codon expression for a particular host," and that the reference also "suggest that the genetic code and species specific codon preferences are well known in the art and it would be routine for one of ordinary in the art to generate degenerate variants described above, to optimize codon expression for a particular host." (OA at page 10.) According to the Examiner Nagata *et al.* teach the use of the *Homo sapiens* codon optimization tables. (OA at page 10.) Hartikka *et al.* teach the use of cationic lipid, for example GAP-DMORIE : DPyPE, to elicit an immune response. Thus, the use of cationic lipid is routine in the art citing Hartikka *et al.* (OA at page 10.) Applicants respectfully traverse this rejection.

The factors to be considered under 35 U.S.C. § 103(a), are the scope and content of the prior art; the differences between the prior art and the claims at issue; and the level of ordinary skill in the pertinent art. *See Graham v. John Deere*, 383 U.S. 1 (1966) and MPEP §2141. This has been the standard for 40 years, and remains the law today. *See KSR International Co v. Teleflex Inc.*, 550 U.S. ___ (2007).

Additionally, in order to support a *prima facie* case of obviousness, the prior art must suggest making the *specific* molecular modifications necessary to achieve the claimed invention. *See In re Deuel*, 51 F.3d 1552, 1558 (Fed. Cir. 1995); *In re Lalu*, 747 F.2d 703, 705 (Fed. Cir. 1984) ("[t]he prior art must provide one of ordinary skill in the art the motivation to make the proposed molecular modifications needed to arrive at the claimed compound."). That is, simply because "one can conceive a general process in advance for preparing an *undefined* compound [*e.g.*, a codon optimized polynucleotide encoding the protective antigen of *B. anthracis*] does not mean that a claimed *specific*

compound. *See In re Deuel* at 1559. Specifically, a polynucleotide encoding a polypeptide "at least 97% identical to amino acids 199 to 764 of SEQ ID NO:4, wherein the amino acids of said polypeptide corresponding to amino acids 192 to 197 of SEQ ID NO:4 have been deleted" which has been codon optimized in a manner specified in independent claims 215, 231, 245, 261 and 275 was not precisely envisioned in the prior art and therefore the composition cannot be obvious. Thus, in order for cited references to be suitable as primary references upon which to base a *prima facie* case of obviousness, there must be, at a minimum, a teaching or suggestion in these references that would have compelled one of ordinary skill in the art to codon optimize a polynucleotide encoding "SEQ ID NO:4, wherein the amino acids of said polypeptide corresponding to amino acids 192 to 197 of SEQ ID NO: 4 have been deleted" as claimed. Especially in view of the numerous potential polynucleotides which could encode for SEQ ID NO:4 with the furin cleavage site deleted and the numerous potential ways to codon optimize the polynucleotides. Therefore, the cited references taken together are seriously deficient (particularly in view of the holding in *Deuel*), and cannot support a *prima facie* case of obviousness.

Independent claims 215, 231, 245 and 261, from which all other method claims depend, recite a method for treating or preventing anthrax infection in a vertebrate "comprising administering to a vertebrate in need thereof a composition comprising a carrier, a lipid GAP-DMORIE, a co-lipid and an isolated polynucleotide comprising a nucleic acid fragment which encodes a polypeptide at least 97% identical to amino acids 199 to 764 of SEQ ID NO:4, wherein the amino acids of said polypeptide corresponding to amino acids 192 to 197 of SEQ ID NO:4 have been deleted . . . " Applicant asserts

that Lee *et al.* does not teach or suggest the administration of a polynucleotide encoding a polypeptide at least 97% identical to amino acids 199 to 764 of SEQ ID NO:4 with the furin cleavage site deleted and were the polynucleotide is codon optimized, as set forth in claims 215, 231, 245, 261 and 275, in combination with the lipid GAP-DMORIE and a co-lipid nor do they suggest or disclose the specific codon optimization recited in the claims.

Lee *et al.* does not disclose SEQ ID NO:4 with the furin cleavage site deleted. The furin cleavage site is made up of the amino acid sequence "SRKKRS" (corresponding to amino acids 192-197 of SEQ ID NO:4). The reference does not disclose a TPA-PA, full length protective antigen, with a deleted the furin cleavage site. Furthermore, Lee *et al.* does not suggest the deletion of the furin cleavage site. Thus, the reference does not teach or suggest a full length PA antigen with the furin cleavage site deleted as required by the present claims. Even though, the reference discloses sequences that are 97 % identical, there is no suggestion to remove of the furin cleavage site found in the reference of Lee *et al.* Thus, the reference does not suggest a composition, let alone a method "comprising administering to a vertebrate in need thereof a composition comprising a carrier, a lipid GAP-DMORIE, a co-lipid and an isolated polynucleotide comprising a nucleic acid fragment which encodes a polypeptide at least 97% identical to amino acids 199 to 764 of SEQ ID NO:4, wherein the amino acids of said polypeptide corresponding to amino acids 192 to 197 of SEQ ID NO:4 have been deleted . . ."

Hartikka *et al.* does not cure the deficiencies of Lee *et al.* Hatikka *et al.* discloses the injection of mice using Vaxfectin formulated with pDNA encoding influenza

nucleoprotein (NP). (Abstract, page 1911.) "The mechanism by which Vaxfectin enhances the antigen-specific antibody response is unclear." (page 1921, column 1, 2nd paragraph.) "Experiments are underway to further characterize the critical features of the Vaxfectin-derived response, and to expand the scope of the application of Vaxfectin adjuvancy for pDNA vaccines to other antigens, tissues, routes of administration and target species." (page 1921, column 2, last paragraph.) Thus, the ordinary artisan after reading Hartikka *et al.* would not have had an expectation of success in using other antigens because the authors clearly indicate that further studies are needed. Additionally, Hatikka *et al.* does not teach or suggest the administration of a codon-optimized polynucleotide encoding a polypeptide at least 97% identical to SEQ ID NO:4 in with a deleted furin cleave site.

Nagata *et al.* does not cure the deficiencies of Lee *et al.* Indeed, Nagata *et al.* discloses the use of a gene encoding amino acid residues 91 to 99 of listeriolysin O (LLO) derived from *Listeria monocytogenes*. The gene was codon optimized for mouse and then used to immunize mice via the gene-gun delivery method. Nagata *et al.* does not teach or suggest the administration of a codon-optimized polynucleotide encoding a polypeptide at least 97% identical to SEQ ID NO:4 with a deleted furin cleavage site administered to a vertebrate in a composition comprising GAP-DMORIE and a co-lipid as claimed.

As such, the combined references cited by the Examiner do not suggest the claimed methods, and specifically claimed molecular modifications. Therefore, Applicant respectfully requests withdrawal of the rejection as it relates to the currently pending claims.

Conclusion

All of the stated grounds of objection and rejection have been properly traversed, accommodated, or rendered moot. Applicant therefore respectfully requests that the Examiner reconsider all presently outstanding objections and rejections and that they be withdrawn. Applicant believes that a full and complete reply has been made to the outstanding Office Action and, as such, the present application is in condition for allowance. If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

Prompt and favorable consideration of this Amendment and Reply is respectfully requested.

Respectfully submitted,

STERNE, KESSLER, GOLDSTEIN & FOX P.L.L.C.

Ulrike Winkler Jenks
Attorney for Applicant
Registration No. 59,044

Date: 6/5/07

1100 New York Avenue, N.W.
Washington, D.C. 20005-3934
(202) 371-2600
682431_1.DOC